Application No. 09/225,233. Accordingly, applicants respectfully request withdrawal of the rejection.

Double Patenting Rejection

Claims 45-56 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11-18 of U.S. Patent No. 6,252,133. Solely to expedite allowance of the pending claims, and not in acquiescence to this rejection, applicants will submit a Terminal Disclaimer in compliance with 37 C.F.R. § 1.321(b) when the claims are otherwise indicated to be allowable.

Rejections under 35 U.S.C. § 102(b)

The pending claims were variously rejected over several publications that teach the production of embryos and mammals. (Massey, 1991; Campbell and Marshall, 1975; Sims et al., 1991; and Stice et al., 1995). Applicants do not agree that this rejection is proper and request reconsideration.

The cited references teach the conventional production of embryos and mammals, i.e., by fertilization of an egg with a sperm, and the use of cells from a conventionally produced embryo for nuclear transfer. As applicants have previously pointed out, conventional reproduction and cloning using a conventional embryo as the source of donor cells are well understood to have a critical limitation: they do not permit one to select an existing mammal that has advantageous characteristics and make a genetic copy of that mammal. In both instances – conventional reproduction and cloning from a conventional embryo – creation of the embryo requires mixing the genetic material of one pre-existing mammal with the genetic material of another pre-existing mammal, i.e., a sperm and an egg. As a result, the embryo, and a mammal

produced from it by nuclear transfer, is an unpredictable mixture of the genetic traits carried by the two parental mammals. The present invention overcomes that limitation by using a differentiated cell taken from the mammal.

In contrast to the cited references, the present invention permits the cloning of a pre-existing mammal by taking a differentiated cell from the mammal. The result is that applicant's clones are clones of a pre-existing mammal. They are, therefore, asexually produced and do not require sexual reproduction. That is, the chromosomes of the claimed clones come from a single pre-existing "parent." That is not the case with the mammals/embryos produced in each of the references – the clones taught are not clones of a pre-existing mammal, but arise from a process involving sexual reproduction. As explained in the attached Declaration of Dr. David Wells under 37 C.F.R § 1.132, two mammals, not one, are the source of the chromosomes of the progeny described in the cited references. There is no single "parent" from which a clone is produced. Consequently, the mammals/embryos described in these references do not have the same set of chromosomes as either one of their parents, but contain a mixture of chromosomes from each parent used to produce the embryo. This, of course, highlights the breakthrough advantage of the present invention: the ability to produce a clone that has the same chromosomes as a selected parent mammal, without having to "dilute" those selected genetics by sexual reproduction.

With specific reference to the pending claims, it can therefore be seen mammals/embryos described in the cited references are not "clone[s]" of a "pre-existing, non-embryonic, non-human mammal from which a differentiated cell has been taken" as recited in applicants' claims. Dr. Wells' declaration attests that the cited references do

not disclose an embryo or mammal that contains the same set of chromosomes as its parental mammal, as recited in applicants' claims.

Applicants do not understand the relevance of the allegation set forth in the Office Action that an embryo or mammal produced by any of the methods of the cited references would "look and behave identically to an embryo or mammal of the present claims." For example, in reference to the Sims article, is the Examiner saying that since a cow cloned by the method disclosed by Sims would look like and behave like a cow, and the cow produced by the present invention would also look like and behave like a cow, then the cow produced by the present invention cannot be patentable? Surely, the issue of patentability cannot turn on how the cow looks and behaves. Rather, it must turn on a point of novelty and non-obviousness, which point must be defined by the claims. That point is found quite clearly in the present claims: Applicants' clones are clones of a pre-existing, non-embryonic mammal from which a differentiated cell has been taken. The Examiner has not cited a single reference that teaches or suggests such clones.

Similarly, the Examiner states that "One cannot simply look at the genome of embryos and discern those genomes that are the result of fertilization and those that are the result of nuclear transfer." Applicants fail to understand the relevance of this observation to the patentability of the claims and would appreciate being guided as to the statutory basis for the requirement for the origin of a composition to be apparent from simple inspection for it to be patentable.

Perhaps, the Examiner is concerned that the casual observer would not be able to tell if a particular mammal were a cloned mammal covered by the claims of this

application. This may be true, and indeed very few patented articles are immediately recognizable as being patented unless they are appropriately marked. However, this issue has been addressed by Congress in 35 U.S.C. § 287, relating to patent marking requirements, which places strict limits on the ability to recover monetary damages for infringement where the product was not marked with an appropriate indication of the patent. The ability of a purchaser to ascertain whether a product is patented is thus indeed a concern, but it is a concern of the courts when determining liability for patent infringement. It is not a concern of the Patent Office when determining patentability, and applicants respectfully submit that it is not a proper basis for rejection of the claims of this application.

The Office Action sets forth at length the position that the claimed embryos have the "same structure, same function, and same developmental potential" as embryos taught in the cited references. The Office Action also contends that "Applicant's embryos and mammals are clones of embryos [that] existed prior to the claimed invention." Applicants do not contest that a cloned cow or a cow embryo clone covered by the present claims will generally look like any other cow or cow embryo, including those taught in the cited references and the "parent" mammals from which the clones of the invention are derived. But this observed similarity cannot be the basis for a novelty or obviousness rejection, since it ignores critical limitations in the claims that are absent from the teachings of the cited references and which distinguish the claimed invention from the parental mammals. Specifically, neither the mammals in the cited references nor the parent mammals of the claimed clones are mammalian clones (or embryo clones) of a pre-existing, non-embryonic mammal from which a differentiated cell has

been taken. This limitation defines a structural characteristic that distinguishes these clones from any mammal or clone of record. It satisfies the requirement reflected in M.P.E.P. § 2113 and summarized by the Examiner as the need for "specific structural or other differences" between applicants' claimed subject matter and the cited art. This limitation clearly satisfies the Examiner's demand for applicants to show "a difference between the embryos of Massey and the presently claimed embryos" as well as between the claimed embryo clones and cloned mammals and the embryos and mammals of Sims, Stice, and Campbell & Marshall. Applicants point out that the limitation is a structural limitation recited in the claims, and is not merely a "process limitation." The Examiner cannot simply ignore this limitation based on the premise that applicants' claims are "product-by-process claims." Withdrawal of the rejection is respectfully requested.

Applicants also point out that the argument set forth in the Office Action that the claimed clones will be indistinguishable from the nuclear donor parent mammals and from the mammals disclosed in the cited references is scientifically incorrect. While all of these mammals will have the general characteristics of their species, they will differ in significant ways that will permit them to be distinguished one from the other, just as any two mammals of the same species can be distinguished. The phenotype of any mammal is determined by the combination of its genetic make-up and environmental factors. *See* Ayala et al., 1980 (submitted with applicants' June 19, 2002, Amendment). Since the presently claimed mammals have different chromosome compositions and are raised in different environments compared to the mammals disclosed in the cited

references, they will quite clearly be distinguishable. The suggestion that all mammals of the same species are indistinguishable is patently wrong.

Furthermore, the structure and composition of an embryo or mammal produced by any of the methods of the cited references would not be identical or substantially identical to an embryo or mammal of the pending claims because their chromosomes would be different. The differences in their chromosomes could be readily distinguished, for example, using the well-known technique of genetic analysis. *See* Declaration of Dr. David Wells under 37 C.F.R § 1.132; *see*, *also,* Glassberg, U.S. Patent 5,593,832 (Exhibit 1) and Erlich, U.S. Patent 4,582,788 (Exhibit 2).

Similarly, the claimed clones are not indistinguishable from the "parent" mammals from which the donor cell was derived. One difference is readily apparent – they will be of different ages. That aside, they will be exposed to different environmental factors and therefore have different phenotypes. Indeed, even clones created from the same donor source have observable phenotypic differences. *See* Declaration of Dr. David Wells under 37 C.F.R § 1.132; *see*, *also,* Prather, Flom et al., and Wells et al. submitted with applicants' June 19, 2002, Amendment.

However, these arguments are secondary to the real issue here which is whether the claims recite a feature that distinguishes the claimed subject matter from the cited art. The pending claims clearly meet this test: nothing in the cited art teaches or suggests a mammalian clone (or embryo clone) of a pre-existing, non-embryonic mammal from which a differentiated cell has been taken.

to discuss any outstanding issues. If there is any fee due in connection with the filing of this Amendment, please charge the fee to Deposit Account No. 07/1139.

Respectfully submitted,

Dated: February 28, 2003

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New Claims 69-71

As noted above, new claims 57-68 are derived from canceled claims 45-56 and emphasize that the claimed embryos and mammals are clones. New claim 69 recites a non-human, non-embryonic mammal from which a differentiated cell has been taken and a clone thereof. The cited references do not disclose the claimed combination. The claimed combination is generated upon the birth of a clone of a pre-existing mammal from which a differentiated cell has been taken, and is not a function of any spatial relationship between the two mammals.

New claim 70 recites a cell culture comprising non-human mammalian differentiated cells and a non-human mammalian clone produced therefrom. The cited references do not disclose the claimed combination. The claimed combination is generated upon the birth of a clone from a pre-existing differentiated cell culture, and is not a function of any spatial relationship between the mammal and the cell culture.

New claim 71 recites a reconstituted non-human mammalian oocyte comprising the nucleus of a differentiated non-human mammalian diploid donor cell from the same species in the G1 phase of the cell cycle, wherein the reconstituted non-human mammalian oocyte is capable of developing to term. The cited references do not disclose such a reconstituted oocyte. Accordingly, new claims 69-71 are not anticipated by the cited references.

Conclusion

Applicants respectfully submit that this application is now in condition for allowance. If the Examiner believes that issues remain to be addressed before a Notice of Allowance, applicants respectfully request that the Examiner contact the undersigned